

REMARKS

With this Reply, Claims 1, 21 and 41 have been amended in order to facilitate prosecution of subject matter that is particularly preferred at this time. Claims 55-64 are canceled in response to a March 13, 2003 Restriction Requirement. After entry of this Reply, Claims 1-54 are pending in the instant Application. Applicant expressly reserves the right to prosecute Claims drawn to canceled subject matter, and to the Claims to subject matter described in the application as originally filed, in one or more continuing applications.

Amendment to the Specification

Paragraph [0065] is amended to correct a typographical error in the term “eexternally” to “internally”. Support for this correction can be found at www.alzet.com which is cited in Specification paragraph [0065] (Appendix, p. 1, col. 2, first paragraph).

Amendments to the Claims

Support for the amendment of Claims 1, 21 and 41 may be found, for example, in the originally filed Claims 18 and 39 and paragraph numbers 0040; 0061; and 0062-0066 of the Specification. Support for new Claims 65-67 may be found in paragraph numbers 0040 and 0061 of the Specification.

No new matter is added by the amendment of Claims 1, 21 and 41 or by adding new claims 65-67. Accordingly, entry into the instant Application is proper and respectfully requested. The claims are drawn to subject matter of the invention that is preferred at this time.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 41 – 64 stand rejected under 35 U.S.C. §102(b) as being anticipated by EP 0 079 405 (hereinafter “Corless”) and United States Patent No. 5,429,602 (hereinafter “Hauser”). A need for a response to the rejection of Claims 55- 64 is obviated by cancellation of Claims 55-64. Applicants traverse the rejection of Claims 41 – 54, particularly in light of the amendments made to Claim 41.

Anticipation of a claim requires that the reference teach every element of the claim.

MPEP § 2131. Thus, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”

Verdegaal Bros. v. Union Oil Co. of California 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The subject matter of one aspect of the instant application is a method for treatment of an interferon responsive disorder in a warm-blooded animal. The method addresses the problem of individualizing doses of interferon for a particular patient. The problems with short-term and long-term administration of interferon are discussed at pages 4 and 5, ¶0012-0016 of Applicant's specification. Applicant's invention as defined in its various aspects maximizes the probability of delivering an effective dose of drug, such as interferon, to treat an interferon responsive disease or condition, and further maximizes the chances of delivering a safe dose of the drug such that the dose is minimally toxic and therefore tolerated by the recipient. The invention facilitates the selection of a safe, tolerated and effective dose of an interferon by a long-term delivery system and facilitates dose individualization of the drug for an individual patient in the setting of the long-term administration using a long-term delivery system. As pointed out in the Specification at page 11, paragraph [0040], the long term delivery will generally involve the delivery of a drug at a more or less fixed rate if the system start-up or shut-down effects, if any, are ignored. A long-term delivery system, for example, may be an internally presented implantable pump such as the DUROS® system. (Specification at page 19, paragraph [0064]) The invention minimizes or eliminates the need to alter the rate or change the dose rate of the drug once long-term dosing has commenced.

To effectuate the method of treatment for individualizing a dose, Applicant claims a method of manufacturing a long-term delivery device for delivering a drug over time. In claim 41, the method comprises two steps. The first is preparing a long-term delivery by device or delivery of the drug at a relatively constant rate which is determined to be a unit rate designed for a patient to receive a standard rate. The second step is preparing a delivery device designed for delivery of the same drug at a relatively constant rate over time, which is a fraction of the standard dosage rate. Each unit dose and/or a fraction dose is then suitable for administration to a patient alone or in combination.

Independent Claim 41 recites, *inter alia*, a “long-term delivery device designed for delivery of a drug at a relatively constant rate over time”. Furthermore, Claim 41 now recites that each device *releases interferon from an implantable pump that is not externally programmed and* is suitable for *internal* presentation to a patient (emphasis added).

Corless teaches a method and an external apparatus for improving blood sugar control in diabetics, including an infusion “system comprising two long-term delivery devices that can deliver drugs at constant rates” (Office Action at Paper 9, page 2, paragraph 3), by using external, adjustable-rate devices. Further, the *external* infusion system requires a tissue access system *connected to the body* of the patient (Corless at page 3, lines 25-26(emphasis added)). Corless discloses that the insulin delivery through the tissue access system may be through the intravenous route, the subcutaneous route, and the intraperitoneal route (Corless at page 7, lines 4-10). Corless fails to teach or suggest that the long-term delivery device *releases interferon from an implantable pump that is not externally programmed* which are required elements of the invention recited in Claim 41. Claim 41 as amended emphasizes the implantability, non programmability and internal presentation aspects of the invention. None of these aspects are addressed by Corless.

Examiner notes that the Corless system could be used “to deliver the same drug at different rates.” The use of two external, adjustable rate systems to achieve what could be achieved with one system would not represent an advance, and Corless has clearly avoided this suggestion. Examiner further suggests that Corless teaching the “delivery of two compounds does not change the nature of the device itself,” Applicant respectfully disagrees on the basis of Corless’ own statements. As Corless makes clear, the only purpose of the second device is to achieve programmable, variable rate dosing of a second agent. Therefore, there would not *be* a second device present were it not for the required presence of a second, distinct agent, a view that Corless makes repeatedly. For example, Corless teaches that a second agent (dextrose) is designed to oppose the action a first agent (insulin) if a patient becomes hypoglycaemic or hyperglycemic (Corless at page 10, lines 1-6)

Accordingly, Corless fails to anticipate independent Claim 41 in that it does not teach every element of the claim. Since Claims 42-54, ultimately depend from Claim 41, Corless also fails to anticipate these claims.

In view of the foregoing, Applicants respectfully request that the rejection of Claims 41-54 under 102 U.S.C. § 102(b) as being anticipated by Corless be withdrawn.

Claims 41-64 stand rejected as being anticipated Hauser, for the reasons set forth for Corless (Office Action at Paper 9, page 3, paragraph 3). Hauser teaches an external infusion pump system that comprises two pumps whereby infusion rates are separately programmable (Office Action at Paper 9, page 3, paragraph 3). Further, Hauser teaches that the *external* portable infusion pump comprises, *inter alia*, an “infusion tube *connected* to a patients body” (Hauser at Column 1, line 13) (emphasis added)). Hauser fails to teach or suggest that the long-term delivery device *presented internally that releases interferon from an implantable pump that is not externally programmed*.

Accordingly, Hauser also fails to anticipate independent Claim 41 in that it does not teach every element of the claim. Since Claims 42-54, ultimately depend from Claims 41, Hauser also fails to anticipate these claims.

In view of the foregoing, Applicants respectfully request that the rejection of Claims 41-54 under 102 U.S.C. §102(b) as being anticipated by Hauser be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 1-3, 8, 10, 14-19, 21-24, 28, 30 and 34-40 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the three-way combination of Palmeri *et al.* J. Chemotherapy 1990, vol. 2(3), pp. 327-330 (hereinafter “Palmeri”) in view of Corless and Hauser. Applicant traverses the rejection of Claims 1-3, 8, 10, 14-19, 21-24, 28, 30 and 34-40.

Applicant respectfully points out that the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. *In re Bell* 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); MPEP § 2142. Accordingly, *inter alia*, the Patent Office must establish that the prior art, either alone or in combination, teaches or suggests each and every limitation of the rejected

claims. *Litton Indus. Products, Inc. v. Solid State Systems* 755 F.2d 158, 164 (Fed. Cir. 1985); *In re Royka* 180 USPQ 580 (CCPA 1974); *In re Wilson* 165 USPQ 494 (CCPA 1970); MPEP § 706.02(j). The teaching or suggestion to make the claimed invention, must come from the prior art, rather than the Applicant's specification. *In re Vaeck* 20 USPQ2d 1438 (Fed. Cir. 1991). If this criteria is not met, *prima facie* obviousness is not established.

Here the Examiner is attempting to combine unrelated art. Corless and Hauser teach external pump apparatuses for administration of drug (e.g. insulin and dextrose in Corless) over time and Palmeri teaches administration by injection of alpha interferon-2a. The Examiner provides no motivational linkage to combine the three. For example, why would a researcher in the area of treating colorectal carcinoma with IFN-2 α (Palmeri) look to the treatment of diabetes with insulin (Corless)?

Palmeri teaches administration of alpha interferon-2a to patients suffering with colorectal carcinoma. The Examiner stated that Palmeri "fails to teach the use of a controlled-release formulations" and that Corless and Hauser teach devices suitable for controlled release. (Office Action at Paper 9, page 4, paragraph 5).

Applicant respectfully submits that that Palmieri teaches only the short-term, discontinuous administration of different dose levels of interferon to *different groups of patients* with cancer (table 3, p. 329). Palmieri teaches only *between-group dose-escalation*. Palmieri (col 1, p 330) does not teach dose-individualization for single patients. In addition, Palmieri teaches only the use of *one formulation* of interferon (which produces highly variable interferon blood levels in cancer patients). Palmieri also does not teach the use of a short-term interferon formulation in conjunction with a long-term formulation to achieve true patient-specific dose optimization.

Contrastingly, the invention recited in independent Claims 1, drawn to a method of treatment, and 21, drawn to a method for individualizing doses, requires that the long-term formulation and long-term delivery system, respectively, release *interferon from an internally presented implantable pump that is not externally programmable*. Palmeri, Corless and Hauser fail to teach or suggest that long-term delivery release of *interferon from an internally presented implantable pump that is not externally programmable*. Accordingly, the combination of

Palmeri, Corless and Hauser fails to teach or suggest the internal long-term formulation and long-term delivery system recited in Claims 1 and 21.

Accordingly Corless and Hauser fail to cure the deficiency of Palmeri to render independent Claims 1 and 21 obvious under 35 U.S.C. §103(a). Since Claims 2, 3, 8, 10, 14-19, 22-24, 28, 30 and 34-40 ultimately depend from Claims 1 or 21, the combination of Palmeri, Corless and Hauser also fails to render these Claims obvious.

In view of the foregoing, Applicant respectfully requests that the rejection of Claims 1-3, 8, 10, 14-19, 21-24, 28, 30 and 34-40 as obvious under 35 U.S.C. §103(a) as being unpatentable over Palmeri in view of Corless and Hauser be withdrawn.

Claims 4-7, 9, 12, 13, 20, 25-27, 29, 32 and 33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Palmeri, Corless, and Hauser in view of Johnson et al. (Scientific American, May 1994, pp.68-75). Applicants traverse the rejection of Claims 4-7, 9, 12, 13, 20, 25-27, 29, 32 and 33.

The Examiner stated that Palmeri, Corless, and Hauser fail to teach the interferons, formulation, or diseases meeting the limitation of the above claims (Office Action at Paper 9, page 5, paragraph 6). Johnson discloses that interferon-alpha may be used to treat chronic hepatitis B and C, hairy-cell leukemia, Kaposi's sarcoma, interferon-beta is used to treat relapsing-remitting multiple sclerosis, and interferon-gamma is used to treat chronic granulomatous disease.(Johnson at page 74).

As established above Palmeri, Corless and Hauser fail to render independent Claims 1 and 21 obvious under 35 U.S.C. §103(a). Since Claims 4-7, 9, 12, 13, 20, 25-27, 29, 32 and 33 ultimately depend from Claims 1 or 21, the combination of Palmeri, Corless, Hauser and Johnson also fails to render these Claims obvious. Further, Johnson also fails to mention release of *interferon from an internally presented implantable pump that is not externally programmable*. In view of the foregoing, Applicant respectfully requests that the rejection of Claims 4-7, 9, 12, 13, 20, 25-27, 29, 32 and 33 under as being unpatentable over Johnson in view Palmeri, Corless and Hauser be withdrawn.

Claims 11 and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Palmeri, Corless, and Hauser in view of U.S. patent 4,847,049 (hereinafter "Kwan"). Applicants traverse the rejection of Claims 11 and 31.

As with the other three references cited by the Examiner, Kwan fails to mention *interferon released from an internally presented implantable pump that is not externally programmable*. Further Applicant has shown above that the combination of Palmeri, Corless and Hauser fail to render independent Claims 1 and 21 obvious under 35 U.S.C. §103(a). Since Claims 11 and 31 ultimately depend from Claims 1 and 21, respectively, the combination of Palmeri, Corless, Hauser and Kwan also fails to render these Claims obvious.

In view of the foregoing, Applicant respectfully requests that the rejection of Claims 11 and 31 under 35 U.S.C. 103(a) as being unpatentable over Palmeri, Corless and Hauser, as applied to Claims 1 and 21 , and in further view of Kwan be withdrawn.

CONCLUSION

Applicant respectfully submits that all pending Claims of the captioned Application satisfy all requirements for patentability and are in condition for allowance. An early indication of the same is therefore respectfully requested.

No fees are believed due in connection with this Reply beyond the Petition to Extend Time. However, the Commissioner is authorized to charge any required fee not included with this Amendment or credit any overpayment to Deposit Account No. 03-3117.

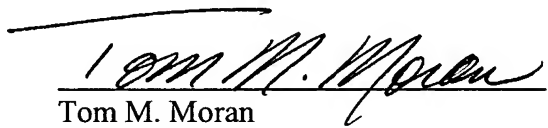
If the Examiner determines that prosecution of the instant application would benefit from a telephone interview, the Examiner is invited to call the undersigned attorney at (650) 843-5104.

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